Isolated Nail Pigmentation Induced by Minocycline: A Case Report

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Abstract
Isolated pigmentation of the nails induced by minocycline therapy is an uncommon occurrence that has only been reported in a handful of cases. In the reported cases of isolated nail discoloration, it has been suggested that nail discoloration may occur preceding other sites of pigmentary changes. As certain types of minocycline-induced pigmentation can be permanent, it is important for clinicians to be aware of this association and discontinue therapy as soon as pigmentary changes are noticed. In this report, we present a case of isolated nail discoloration in the setting of prolonged minocycline therapy for the treatment of rosacea.

Keywords: Minocycline, drug reactions, general dermatology, cosmetic dermatology, hyperpigmentation

Introduction

Minocycline is a second-generation tetracycline antibiotic that is commonly prescribed by dermatologists to treat skin conditions such as rosacea and acne. Hyperpigmentation of the skin, eyes, oral mucosa, and teeth is a well-documented, but uncommon side effect of minocycline, with nail pigmentation being less common [1,2]. To our knowledge, only a handful of cases of isolated nail pigmentation induced by minocycline have been reported [3]. Herein we present a case of isolated minocycline-induced nail pigmentation in a patient being treated for rosacea.

Case Presentation

A 62-year-old Caucasian female with history of Sjogren's syndrome, systemic lupus erythematosus, and rosacea presented to the clinic for fingernail discoloration of six-months duration. Physical examination revealed asymptomatic slate-blue dermal hyperpigmented patches in the proximal nail beds of all 10 fingernails (Figure 1). No additional areas of hyperpigmentation were identified. Medication reconciliation was notable for minocycline dosed at 100 mg daily for several years for the treatment of papulopustular rosacea. Minocycline-induced hyperpigmentation was determined to be the most likely cause given the nail discoloration occurred during a prolonged course of minocycline therapy. Minocycline was discontinued and the patient was counseled that the hyperpigmentation may take months to years to fade or may remain permanent.

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Discussion

For the last 50 years, dermatologists have prescribed minocycline for the treatment of acne, rosacea, and many other cutaneous conditions [4]. Although pigmentation of the teeth, skin, eyes, and oral mucosa is a well-documented but rare side effect of minocycline therapy, isolated pigmentation of the nailbeds is exceedingly rare [1-3]. Pigmentation of the nails can potentially precede the development of additional areas of pigmentation, making this an important clinical finding for clinicians to be aware of [3]. Although the data is limited, published reports suggest that 3-15% of patients on cumulative doses of minocycline greater than 100 mg will develop discoloration in at least one site, with multiple sites of discoloration being more common [1-3]. The etiology of minocycline-induced pigmentary change is unknown, however it may be related to polymerized reactive metabolites, insoluble chelation products, and prolonged treatment courses [5]. Four types of minocycline-induced pigmentation have been described [2]. Type I is the most common type and is described as blue-black discoloration in areas of existing scarring or active inflammation [2,6]. This type most commonly occurs in facial acne scars and is thought to result from deposition of iron-chelated complexes of minocycline in the dermis [2]. Type II is described as blue-grey discoloration of previously normal skin, commonly on the forearms and shins [2]. On histology, pigmented metabolites of minocycline have been found in dermal macrophages or scattered freely within dermal collagen [2,6]. Type III, the least common type, consists of dirty brown discoloration of sun-exposed areas and is associated with increased melanin deposition in both epidermal and dermal macrophages [2]. Type IV is closely related to type III, but only occurs in areas of existing scarring and is not limited to areas that are exposed to the sun [2]. Of the four reported types of minocycline-induced pigmentation, types I and II are more likely to slowly resolve after discontinuation of the drug. Interestingly, type III is associated with permanent discoloration despite discontinuation of therapy [2,6]. The nail pigmentation described in this patient is most consistent with Type II minocycline-induced pigmentation.

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This case underscores the importance of routine nail examination in patients receiving minocycline therapy, especially in those requiring prolonged courses of the drug. It is important to note that minocycline dyspigmentation may occur early or after prolonged use and as such clinicians and pharmacists should counsel patients on this risk even if used for short courses. Furthermore, because additional areas of pigmentation may develop later during therapy, it is essential that minocycline is discontinued at the first sign of nail discoloration. Clinicians and pharmacists should be aware that other tetracycline antibiotics, such as doxycycline, may be used as an alternative therapy because they lack the associated risk of pigmentary changes.

We recommend that minocycline be discontinued immediately upon recognition of pigmentary changes and initiating doxycycline as an alternative therapy. The patient should be counseled to avoid minocycline in the future and to complete regular self-skin examinations to monitor for development of additional areas of dyspigmentation. Clinicians should inform the pharmacist upon changing therapy from minocycline to doxycycline as part of team-based management of this condition. Continuity of care is vital as the dyspigmentation can persist for months to years after discontinuation of minocycline. We recommend that the patient have close follow-up every three-months with photo-documentation to evaluate for regression of the pigmentary changes. Should hyperpigmentation persist or develop in other areas, we recommend initiating Q-switched laser (Nd: YAG) therapy, which has been shown to improve the condition [2].

Conclusion

Minocycline induced pigmentary changes typically occur during a prolonged treatment course and most commonly involves the skin, lips, teeth, gingiva, conjunctiva, and sclera. Isolated nail dyspigmentation is rare and may be the presenting clinical location prior to development of pigmentary changes elsewhere. It is important for practitioners to be aware of this finding so that minocycline may be discontinued prior to the development of additional areas of dyspigmentation and potential irreversible pigmentary changes.

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Figure 1: Slate-blue dermal hyperpigmented patches present in the proximal nail beds of all 10 fingernails.

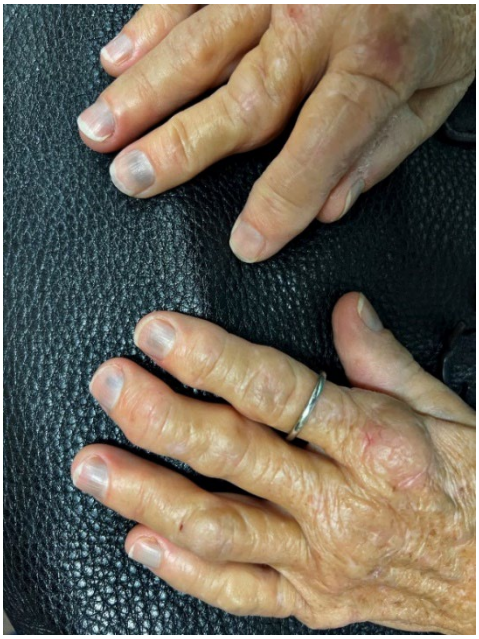

Image provided by Austin Ambur, DO at Advanced Dermatology and Cosmetic Surgery, Orlando, FL

Table 1: Subtypes of minocycline-induced pigmentation clinicopathological findings

Type of Minocycline- Induced Pigmentation	Clinical Findings	Histopathologic Features
Type I	Blue-black discoloration in areas of existing scarring or inflammation; commonly in facial acne scars[2]	Iron-chelated complexes of minocycline deposited in the dermis[2]; Perls' iron/Fontana-Masson melanin stain positive[7]
Type II	Blue-grey discoloration of previously normal skin; commonly the shins & forearms[2]	Pigmented metabolites of minocycline in dermal macrophages and/or scattered freely within dermal collagen[2,6]; Perls' iron/Fontana-Masson melanin stain positive[7]
Type III	Dirty-brown discoloration of sun-exposed skin; most likely of the four types to lead to permanent discoloration[2,6]	Increased melanin deposition in epidermal and dermal macrophages[2]; Fontana-Masson stain positive only[7]
Type IV	Dirty-brown discoloration of skin; not limited to sun-exposed areas[2]	Not described in the literature